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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/828,317	04/06/2001	Craig A. Stump	20620Y	5645

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MERCK AND CO INC
P O BOX 2000
RAHWAY, NJ 070650907

EXAMINER	
BERNHARDT, EMILY B	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 05/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/828,317	STUMP ET AL.	
	Examiner	Art Unit	
	Emily Bernhardt	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *15-19,21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,6,7,9-14,20,23 and 24* is/are rejected.

7)☒ Claim(s) *4,5 and 8* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-14,20,23 and 24, drawn to compounds, simple compositions and use for treating cancer where Z=aryl, classified in class 544, subclasses 362,368,370; class 514 subclasses such as 253.04, etc.

II. Claims 1-3,6,7,9,10,12,13,20,23 and 24, drawn to compounds, simple compositions and use for treating cancer where Z=heterocycle, classified in classes, subclasses as may be determined by the nature of het ring at Z – class 540, various subclasses for azepines; class 544, subclass 238 for pyridazines; class 544, subclass 295 for pyrimidines and many other subclasses.

III. Claims 15-19, drawn to additional uses employing compounds of I, classified in class 514, subclasses various.

IV. Claims 15-19, drawn to additional uses employing compounds of II, classified in class 514, subclasses various.

V. Claims 21-22, drawn to treating cancer employing compounds of I/II and additional antineoplastic agenrs, classified in class 514, subclasses

various as determined by the exact nature of active ingredients to be employed.

If V is elected applicants must pick an ultimate species pair of active ingredients.

The inventions are distinct, each from the other because of the following reasons: Groups I and II pertain to a variety of compounds which contain a diversity of functional groups at either end of the piperazine terminus which are variously classified and would be expected to raise differing issues of patentability. Each can support a patent as they are made and used independently of each other and are not art-recognized equivalents.

Inventions I/II and III/IV are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case more than one use exists as evidenced by the many uses being claimed.

Claim(s) directed to inhibiting prenyl transferases have been grouped with I and II.

Within group V there is more than one invention as the claim recites multiple combinations which require independent searches. Such claims would raise different issues of patentability as additional consideration for compliance with 35 USC 112, most notably the question of sufficiency of dosage regimens that are commensurate in scope with all pairs of active ingredients embraced .

During a telephone conversation with Mr. Muthard on 5/13/04 a provisional election was made without traverse to prosecute the invention of I, claims 1-14,20,23 and 24. Affirmation of this election must be made by applicant in replying to this Office action. Claims 15-19 and 21-22 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

The examiner has required restriction between product and process claims namely **Groups I/II and III/IV**. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP 1 821.04. Process claims that depend from or otherwise include all the limitations of the patentable product will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not

be rejoined. See Guidance on Treatment of Product and Process Claims in light of In re Ochiai, In re Brouwer and 35 U.S.C. 1 103(b), 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. Failure to do so may result in a loss of the right to rejoinder.

Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP ' 804.01.

The abstract of the disclosure is objected to because it does not convey structural makeup of piperazines being claimed. Correction is required. See MPEP 608.01(b).

Claims 1-3,6,7,9-14,20,23-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1.Scope of "aryl" in the claims is not clear. While specification includes phenyl and naphthyl and other rings as possible rings the term "stable" used to

modify scope in the specification is not clear as no guidance is given what sort of stability is intended.

2.The same remarks made in reason #1 also applies to the scope of "heterocycle", "heteroaryl" throughout the variables and claims.

3. Method claims 9-11 are of indeterminate scope for more than one reason. How does one determine who is in need and who is not of inhibiting any and all prenyl transferases? One may have no visible symptoms and still be in need. It may turn out with further research that everyone is in need or that one only needs a specific type among the many types that exist. What cutoff point determines successful inhibitory activity? Specification provides no guidance.

Claims 1-3,6,7,9-14,20,23 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

1. Specification is not adequately enabled for the scope of piperazines claimed which have a variety of functional groups including diverse heteros at many if not all of the R variables as well as Z and V. Starting material sources for such a scope are not seen but are required. Note In re Howarth 210 USPQ 689; Ex parte Moersch 104 USPQ 122. Compounds made and tested which represent the

scope of claim 4 and 5 are directed to a very homogeneous group of compounds with V always being phenyl with CN and/or halo substitution thereon with methanoyl as a link at C(R1a)X with pierazine ring being oxo-substituted with alkyl or thienylmethyl as additional substituents thereon and Y a direct bond or methylene and Z a phenyl ring that is substituted with Cl and/or alkoxy, alkenyloxy. There is no reasonable basis for assuming that the myriad of compounds embraced by the claims will all share the same physiological properties since they are so structurally dissimilar as to be chemically non-equivalent and there is no basis in the prior art for assuming the same. Note In re Surrey 151 USPQ 724 regarding sufficiency of disclosure for a Markush group. Also see MPEP 2164.03 for enablement requirements in cases directed to structure-sensitive arts such as the pharmaceutical art. Also note the criteria for enablement as set out in In re Wands cited in MPEP 2164.01(a), August 2000 edition. Thus given the breadth of the claims which is enormous, the level of unpredictability in the art which is physiological in nature and thus unpredictable, the state of the prior art (no compounds having such a substitution pattern is seen in the prior art) and the lack of direction (i.e. working examples) provided as to what other derivatives might work (compounds tested too homogeneous to evaluate structure-activity

trends for functional groups permitted by the claim language), this rejection is being applied.

2. Method claims directed to inhibiting prenyl transferases and for treating cancers (claims 9-14 and 20) are not enabled for treating all cancers. References (such as Williams provided herewith) directed to prenyl transferase inhibitors , most notably farnesyl transferase (FT) inhibitors which applicants' compounds are, have reasonably correlated FT inhibition to the treatment of ras-dependent tumors which would not be objected to.

Claims 4,5 and 8 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Emily Bernhardt whose telephone number is (571) 272-0664.

If attempts to reach the examiner by phone are unsuccessful, the supervisor for AU 1624, Dr. Mukund Shah, can be reached at (571)272-0674.

The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

E Bernhardt

EMILY BERNHARDT

PRIMARY EXAMINER

Group 1600